cally abnormal findings, including an elevated creatine kinase, raised liver enzyme levels and diffuse slowing seen on the electroencephalogram. No structural abnormalities in the central nervous system have been found in autopsy studies. Death occurs in 20 percent of the cases—usually due to respiratory failure—and 50 percent of these have been related to the use of long-acting phenothiazines. Other serious complications include thromboembolism, aspiration pneumonia, cardiovascular collapse, renal failure and irreversible brain damage.

The underlying causative physiologic mechanism of this disorder is unknown, but speculation relates it to dopamine blockade in the basal ganglia and hypothalamus. Predisposing factors may include organic brain disease, dehydration or physical exhaustion.

Athough there have been scattered reports of treatment success with antiparkinsonian agents, there is currently no known treatment that can reverse the syndrome in most cases. Palliative measures include cessation of administration of the neuroleptic agent and supportive medical care. Because the most effective treatment, then, is prevention, clinicians should prescribe neuroleptic medication only when the benefits outweigh the risks in a psychotic patient.

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Underdiagnosis of Bipolar Disorder: Causes and Implications

NUMEROUS STUDIES, especially during the past decade, have resulted in redefining the criteria for differential diagnosis of various psychiatric disorders, especially for distinguishing the major affective disorders from the schizophrenic disorders. Observations suggest, however, that clinical practice does not yet fully reflect these redefinitions, with cases of bipolar disorder, especially the manic type, continuing to be diagnosed and therefore treated as schizophrenia. The consequences of such a misdiagnosis are several and can be tragic: (1) there is greater social stigma attached to the label of "schizophrenia" than to "bipolar disorder" (manic-depressive disorder), (2) there are poorer prognostic implications of a diagnosis of schizophrenia and a more negative effect on a patient, the family and treatment personnel (that is, "Once a schizophrenic, always a schizophrenic") and (3) often treatment is with agents that are less effective and have the potential for more both short-term and long-term deleterious effects.

Multinational studies in Western Europe have established an approximate 1:1 ratio of schizophrenia to bipolar disorder among hospital admissions. This ratio was confirmed by a study in the United States and Great Britain, indicating that the actual patient types did not differ in the two countries. Various studies have shown, however, that American psychiatrists have diagnosed schizophrenia as much as 8 to 12 times as frequently as bipolar disorder. Recent data from California suggest that underdiagnosis of affective disorder relative to schizophrenia is continuing, though the trend is toward the 1:1 ratio.

Pertinent to the underdiagnosis of bipolar disorder in this country has been the adage "even a trace of schizophrenia is schizophrenia," supported by a diagnostic approach that has relied on a cross-sectional view of signs and symptoms. The *Diagnostic and Statistical Manual of Mental Disorders, 2nd Ed,* which was in use until 1980, used such slice-in-time descriptions and additionally required that for a diagnosis of affective reaction any disturbance of thought or behavior must be consonant with the primary disorder of mood. Therefore, the presence of any mood-incongruent psychotic features excluded the diagnosis of an affective disorder. Subsequent to this edition, research has clarified the nonspecificity of many of the "schizophrenic" symptoms, including mood-incongruent hallucinations and delusions, thought disorder and catatonia. The entire range of "schizophrenic" symptoms has been noted in 20 percent to 50 percent of both manic and depressed patients. The presence or absence of affective symptoms, the family history (for schizophrenia and affective disorder particularly), the premorbid personality and the course of illness are more specific diagnostic indicators. Age of onset is not the differentiating criterion once thought; it is now recognized that bipolar disorder can occur in childhood and adolescence and that such cases tend to have a higher genetic loading and a less favorable course.

The third edition of the above-mentioned manual, now in use, provides specific diagnostic criteria, rather than cross-sectional descriptions, and incorporates many of the findings of recent research in the criteria for distinguishing the schizophrenic disorders and the affective disorders. The trend in the California findings may well reflect increasing familiarity with these criteria. A category of schizoaffective disorder remains, without diagnostic criteria, for those instances in which a clinician is unable to make the differential diagnosis with any degree of certainty; it is not, however, as was formerly the case, included among the schizophrenic disorders but under a new category of "psychotic disorders not elsewhere classified." Such instances emphasize the need for careful diagnostic evaluation as an ongoing process.

In those instances in which the differentiation between a schizophrenic illness and an affective illness featuring manic symptoms is not clear, it is appropriate to institute a trial of lithium carbonate treatment. Such is particularly the case when response to neuroleptics is not satisfactory. The duration of such a trial, barring the development of adverse reactions, should be at least a month at adequate serum concentrations. Research

indicates that lithium is as effective in manic patients with "schizophrenic symptoms" as in those without.

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Ergot Alkaloids and Dementia

ALTHOUGH CLINICIANS have remained sceptical about the use of dihydroergotamine mesylate in treating senile dementia, it remains the only drug approved by the Food and Drug Administration (FDA) for use in "selected symptoms in elderly patients." Recent research findings may lead the way to more effective clinical use of this medication.

Historical review of studies of dihydroergotamine mesylate shows a general tendency for medication dosage to increase, starting with 1.5 mg per day in the early 1950s, to doses of 6, 9 and 12 mg a day at present. The dosage usually prescribed in the United States is 3 mg a day, whereas in Europe 4.5 mg a day is prescribed. In general, those studies done at higher doses report superior efficacy for the high-dose regimen. Of particular interest is a recent direct comparison of 3 mg versus 6 mg a day in more than 500 patients with cerebrovascular disease that found clear superiority for the higher dose.

Such studies improve our knowledge of dosage for dihydroergotamine mesylate but do little to improve our understanding of the rationale for its use. Proposed effects have shifted from improvement of cerebral circulation to effects on cerebral glucose metabolism to, most recently, neurotransmitter effects. Examining the recent comparison of 3 mg versus 6 mg leads to the question of why a drug with supposed effects on neurotransmitters has positive effects in a disease where the cause is structural—that is, cerebrovascular accident—or in other degenerative diseases of the brain. The behavioral rating subscales with greatest improvements were heavy-headedness, loss of concentration and loss of vigor. These results suggest that the drug probably has a positive effect on arousal and attention. Thus it may be that even with structural damage some improvement may be attained in clinical status by increasing aspects of the alertness-arousal-attention complex that may be mediated through other neural systems not injured by the initial attack.

The use of drug concentration determinations and biochemical tests to predict drug response is a fruitful area of research. Much has been written in the general psychopharmacologic literature about the use of metabolites of biogenic amines such as 3-methoxy-4-hydroxyphenylglycol (MHPG) to predict response to antidepressant medications. It has been well documented that major changes occur in biogenic amines with normal aging and also with neuropsychiatric diseases such as dementia, commonly found in the elderly. To date there has been only one preliminary study—by Samorajski and associates—correlating changes in serum prolactin with symptomatic improvement with dihydroergotamine mesylate treatment. This study examined the hypothesis that this ergoloid mesylate's therapeutic effect is related to its dopamine-agonist effects and that serum levels of prolactin fall with increasing agonist activity. Many other biochemical markers remain unexamined as predictors of psychopharmacologic treatments in the elderly with depression and dementia.

In conclusion, encouraging results indicate that doses higher than the FDA-approved 3 mg a day are potentially more beneficial. Further work will need to be done to document these dosage effects on populations in the United States and to further explore potential biochemical predictors of drug response and the benefit of combined therapy.

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Recent Developments in the Diagnosis of Childhood Depression

DEPRESSION IN CHILDREN has long been an area ignored by researchers. This has changed significantly in the past ten years as recent biologic and clinical advances in the study of adult depression have been duplicated in studies of childhood depression.

Several researchers have been working to obtain a consistent set of diagnostic criteria for childhood depression. The *Diagnostic and Statistical Manual of Mental Disorders, 3rd Ed* in 1980 stated that a child must either show a dysphoric mood or a pervasive loss of interest in almost all usual activities, in addition to at least four of the following eight symptoms: (1) change in appetite, (2) sleep difficulty, (3) psychomotor agitation or retardation, (4) loss of pleasure in usual activities, (5) loss of energy, (6) feelings of self-reproach or guilt, (7) complaints or evidence of diminished ability to concentrate and (8) recurrent thoughts of suicide or death. The duration of these symptoms must be longer than two weeks. It has been emphasized that though these criteria offer the advan-